EXTERNAL DATA MONITORING COMMITTEE

C459

Investigational BNT162 Vaccine Program

PF-07302048

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APPENDICES

1. INTRODUCTION

This External Data Monitoring Committee (E-DMC) (hereafter referred to as "the committee") is a single, external, independent, expert advisory group established to oversee safety and efficacy data from the BNT162 Vaccine Program. The primary rationale for establishing the committee is to make certain that appropriate external safeguards are in place to help ensure the safety of subjects and to maintain scientific rigor and study integrity while the trial is on-going.

Pfizer is responsible for conducting this study. BioNTech is the regulatory sponsor of this study.

1.1. Study Design

The COVID-19 program is being developed to address the pandemic crisis which has spread globally at high speed. There are currently no vaccines to prevent infection with SARS-CoV-2 or antiviral drugs to treat COVID-19.

Given the rapid transmission of COVID-19 and incidence of disease in the United States and elsewhere, the rapid development of a safe and effective vaccine is of utmost importance. In the COVID-19 vaccine program, the safety and tolerability of the BNT162 vaccine candidates will be evaluated by assessing prompted local injection-site reactions and systemic events, as well as adverse events and serious adverse events. Predefined stopping rules may be used to ensure safety of study subjects and guide dose escalation and participants may also undergo hematological and chemistry evaluation as defined per protocol. These procedures are described in detail in each study protocol where relevant. The background of the COVID-19 vaccine candidates and pre-clinical development is described in the BNT162 COVID-19 Investigator Brochure (IB). The updated IB will be provided to the committee when available.

Please refer to the current study protocols for details of the study design.

1.2. Purpose of the Committee

The committee will review accumulating safety data across all studies, as well as efficacy data in the Phase 2/3 portion of the C4591001 study. The committee will advise Pfizer regarding the safety of current participants and those yet to be recruited, as well as the continuing scientific validity of the trial. In addition to safety review by the committee, qualified Pfizer personnel will review safety data as specified in the safety surveillance review plan and will inform the committee of significant findings. Efficacy data from the C4591001 study will be available to the committee when there is a planned interim analysis of efficacy or if this is considered necessary to conduct a risk-benefit assessment.

1.3. Committee Close-Out

The committee will have completed its work and been dissolved when it has reviewed final safety data from the last study within the scope of this charter.

2. COMMITTEE MEMBERSHIP

The committee consists of a chairperson and 2-4 additional members, as indicated in the list of members in Appendix 1 *Committee Membership Log* including at least one with medical qualifications and at least one other who is a statistician.

During the conduct of the study, membership of the committee may change based on expertise needed, availability, and new conflicts of interest that warrant a change. A dated log must be maintained in Appendix 1 reflecting any changes in membership. Committee membership is to be for the duration specified in each member's contract. If any member leaves the committee, Pfizer will promptly appoint a replacement in consultation with the committee chairperson, if needed.

2.1. Conflicts of Interest

The committee members will complete a CT22-GSOP-RF01 *Independent Oversight Committee Member Conflict of Interest Form*. Committee members should be free of apparent significant conflicts of interest. Any potential conflict of interest that develops during a member's tenure on the committee must be disclosed by the committee member. Pfizer will determine if any potential conflict requires termination of committee membership.

Each time the committee meets, the study team will ask the committee members to consider whether or not any changes in their conflict of interest status have emerged. Status must be recorded in the committee open meeting minutes and any potential conflicts must be reported using CT22-GSOP-RF01.

2.2. Confidentiality Agreement/Contract

A written agreement (i.e., contract, including confidentiality agreement) must be in place for each external committee member before any services are rendered. No communication, either written or verbal, concerning the deliberations or recommendations of the committee will be made outside of the committee without approval of Pfizer, except as provided for in this charter (refer to Section 6 *Communication Plan Between Pfizer and the Committee*).

2.3. Authorship

A committee member must not be an author of a publication emanating from any study on the BNT162 vaccine program for which they are a member.

3. ROLES AND RESPONSIBILITIES

3.1. Committee Members

The primary responsibilities of the committee members are:

- Review, endorse, and implement the charter.
- Assess the safety data from the study on a regular basis (refer to Section 4.1 *Meeting/Schedule Frequency*) throughout the duration of the trial.
- Assess efficacy data for efficacy and/or futility during Phase 2/3.
- Provide an informed risk-benefit assessment and advise Pfizer regarding the continuation of the trial based on the reviewed data.
- Provide guidance, where appropriate, on additional questions presented by the study team prior to review meetings.
- Adhere to agreements related to potential conflicts of interest.

3.2. Committee Chairperson

The primary responsibilities of the committee chairperson are:

- Review and approve the charter on behalf of the committee members.
- Facilitate discussion by integrating differing points of view and moving the committee towards recommendations to be provided to Pfizer in a timely fashion.
- Prepare closed session meeting minutes (or via a designee).
- Complete CT22-GSOP-RF11 *Brief Recommendation Form* and submit to the study team, according to the communication plan (refer to Section 6 *Communication Plan Between Pfizer and the Committee*).
- Communicate with the study team according to the communication plan on behalf of the committee (refer to Section 6 *Communication Plan Between Pfizer and the Committee*).
- Provide all written records to the study team for archiving.

3.3. Committee Liaison

The committee liaison is not a member of the study team for any study being reviewed by the committee. The committee liaison is designated by Pfizer and will maintain independence

from the study team for the duration of the trial. The primary responsibilities of the committee liaison are:

- Serve as the primary liaison between the committee and Pfizer management.
- Receive and distribute, according to the communication plan, the committee recommendations from the committee chairperson.
- Ensure the committee has access to timely information about the study.
- Handle and maintain a record of communications between the committee and Pfizer.
- Manage written records (e.g., closed session meeting minutes and CT22-GSOP-RF11) between the committee and Pfizer throughout study conduct.

3.4. Reporting Team

The reporting team is designated by Pfizer and is comprised of a reporting statistician and reporting programmer(s). For the Phase 2/3 portion of C4591001 study a medical monitor and clinical scientist is also part of the reporting team. The reporting team are not members of the study team for any of the studies being reviewed by the committee and who will maintain independence from the study team for the duration of the trial. The primary responsibilities of the reporting team are:

- Compile and provide unblinded output to the committee for review.
- Write the closed committee report, including a textual summary of unblinded findings.
- Coordinate appropriate operational support activities from a dedicated team, including a reporting programmer(s).
- Maintain copies of the review meeting materials for each meeting in a secure area with restricted access.
- Serve as the primary contact for all data-related issues. If the committee requires additional data, the request and supporting rationale will be made via email to the reporting statistician (who may elect to consult with the designated Pfizer management). Once the request is agreed, the reporting statistician will provide the data/output to the committee.
- During the Phase 2/3 portion of the C4591001 study the unblinded medical monitor will conduct ongoing review of COVID-19 illness cases.

3.5. Study Team

The study team includes clinician, clinical lead, study statistician, and safety risk lead, and other team members as appropriate. The primary responsibilities of the study team are:

- Ensure qualified study team personnel are available to review blinded (if applicable) safety data per the safety surveillance review plan for the duration of the trial in order to complement the committee's safety role and fulfill Pfizer's obligation to monitor patient safety.
- Select the committee chairperson and members.
- Ensure appropriate study conduct and preservation of the study blind (if applicable) to ensure overall study integrity is maintained.
- Document in a written agreement (e.g., contract) the terms of each committee member's participation and indemnifying all committee members.
- Appoint the committee liaison.
- Appoint the reporting team (including statistician, reporting programmer[s] and medical monitor) not associated with the study team.
- Prepare open session meeting minutes.
- Ensure that all written records are filed appropriately in the Trial Master File (TMF).
- Prepare and implement the committee charter.
- Provide to the committee the study protocol (and any subsequent protocol amendments).
- Notify the committee of any significant new safety information (e.g., toxicology information, potential safety signal, and data from other clinical trials).
- Implement the committee recommendations once endorsed by Pfizer management.
- Promptly review and respond to all committee recommendations and provide the committee with a summary of actions taken in response to its recommendations (as described in Section 6.2 *Communication of Recommendations*).
- Maintain committee records other than closed session meeting minutes and CT22-GSOP-RF11 throughout study conduct.

- Archive all records at the end of the study.
- Submit the committee charter to the Food and Drug Administration (FDA) and other regulatory authorities (RA) when appropriate.
- Organize and facilitate committee meetings, including logistical support such as identifying meeting dates and locations and providing assistance with travel arrangements.

4. COMMITTEE MEETINGS

4.1. Meeting Schedule/Frequency

A start-up meeting (refer to Section 4.2 *Start-up Meeting*) will be scheduled with the committee and members of the study team.

The first committee meeting to review study data will be scheduled no later than within the first month of the first participant dosed with BNT162 vaccine candidates and sooner if needed.

Thereafter, the committee will meet in person or via teleconference as required by the protocol to review cumulative safety data, efficacy data at the time of interim analyses and to make risk-benefit assessments until the study in the program is complete or at intervals determined based on availability of key study data. It is anticipated that regular scheduled meetings will occur approximately monthly. The frequency of DMC meetings may decrease (with agreement between Pfizer and the DMC) as the COVID vaccine program matures however no fewer than two meetings per year will be scheduled.

During Phase 2/3 portion of the C4591001 study, the meeting frequency for cumulative data review will be determined based on availability of key study data. DMC meetings may occur weekly and DMC members will be expected to convene at short notice due to the accelerated pace and critical need of the study if required. The chairperson and Pfizer have the discretion to change the meeting frequency (e.g. if enrollment is slow) or request additional *ad hoc* meetings with the rationale documented appropriately.

4.2. Start-up Meeting

As soon as possible after the committee is formed the committee members, the reporting statistician, and members of the study team will meet to discuss the operational details of the committee and the C4591001 protocol. The committee will review and provide input on Pfizer's proposals for data to be monitored, frequency of reviews, methods for review, and criteria for making recommendations to Pfizer.

The committee members, the reporting team, and members of the study team will meet initially to agree on:

- Data and frequency of data outputs to be provided to committee members outside of planned meetings
- Study conduct issues of interest during review meetings,
- Data elements and statistical methods to be included in safety and efficacy review(s),
- List of tables, listings, and figures and mock-ups,
- Procedural issues such as meeting frequency and format, timing of data receipt and format (including table layouts), definition of a "quorum" (comprising of the Chair, Statistician and one Clinician) and handling of meeting documentation, and
- Criteria and process for unblinding the data and maintaining confidentiality of unblinded results (in the case of a blinded trial or an open-label trial in which the dissemination of such information is restricted).

For E-DMCs established for safety monitoring, the charter must be approved before first subject first visit (FSFV). (It is permissible to meet this requirement with approval of a *preliminary* version of the charter; in this situation, the subsequent version of the charter must be approved before the first scheduled time the committee views unblinded data from the trial.)

For all other E-DMCs the charter will be finalized and approved prior to the first review meeting.

4.3. Review Meetings

The committee will convene to review study conduct and safety data at determined intervals after the start-up and initial safety review meetings. The frequency of meetings will be dependent upon availability and nature of data to be reviewed and will be agreed between Pfizer and the Chair. Additionally, the committee will convene to review data on an as-needed basis (e.g., a stopping rule is met, to review reports of COVID-19-like illnesses, unexpected potential safety signal or study conduct concerns). Data listings and summaries will be supplied to committee members by the reporting statistician via secure electronic means at least 24 hours prior to the meeting but may be up to 5 days prior if possible. The study team will present relevant information on new studies prior to the delivery of the first dataset for these studies.

4.4. Review Meeting Format

Each review meeting will consist of an open and a closed session (when needed). The committee and study team will be unblinded during Phase 1 of the C4591001 study (to identify preferred vaccine candidate(s), dose level(s), number of doses and schedule of administration) but not during Phase 2/3 (expanded cohort and efficacy part). No separate open and closed sessions will be required until the study reaches Phase 2/3 (expanded cohort and efficacy part) including other studies in the program.

These sessions will correspond with the type of briefing materials the committee will receive.

4.4.1. Open Session

The open session provides an opportunity for the committee to interact with members of the study team as applicable, for example to review study status, to discuss dose-escalation decisions made by the IRC, and to discuss AEs that met the stopping rule criteria as applicable. In addition, issues relating to the conduct of the study/studies, potential impact of external data on the study/studies, or other topics defined in the open session of the briefing materials can be discussed.

4.4.2. Closed Session

The closed session is the portion of the meeting where the committee discusses any unblinded results, deliberates over any issues, and votes on recommendations to Pfizer. Only committee members attend the closed-session meeting; however, the reporting statistician and/or the committee liaison may attend all or part of the closed-session meetings with concurrence of the committee chairperson.

Debriefing session

Following the closed session, the committee will meet again with Pfizer representatives to relay comments made by the committee.

4.5. Voting Procedure

All committee members are voting members and are expected to participate in all meetings and voting forums. Every effort should be made in scheduling meetings to ensure that all members can participate. If all members are unable to participate in a meeting, the chairperson and at least one additional clinician must participate in voting. Discussions and decisions requiring expert statistical interpretation of study data require that every effort be made to include the committee statistician. Discussions and decisions regarding pause or termination of study vaccination require that every effort be made to include all committee members. In the event of a split vote, the chairperson will make the final decision concerning the committee's

recommendation. If the chair cannot participate, he/she will delegate his/her role to another member of the committee.

At each meeting, the committee members will vote and provide one of the recommendations listed in Section 6.1 *Recommendations*.

The recommendations regarding the primary endpoint should be in accordance with the guidance provided in this charter, the protocol, or the SAP (or other document, as appropriate, e.g., interim analysis plan).

4.6. *AD HOC* Meetings for Emergent Safety Data

In the event that the committee is convened for an *ad hoc* meeting to evaluate emergent data, processes other than those outlined in this charter may be undertaken on the recommendation of and/or with the express consent of the committee chairperson in order to ensure patient safety within the trial. Any alternative processes will be documented and justified in the committee meeting minutes. In some instances, when not all committee members are able to attend at short notice, it is expected that a minimum of 3 members will meet. At each meeting, the committee members will vote and provide one of the recommendations listed in Section 6.1 *Recommendations*.

4.7. Meeting Minutes

The committee chair is accountable for closed session meeting minutes and may delegate the act of recording minutes during the meeting. Committee members will review and agree to the minutes before they are finalized. At a minimum the minutes should record the following information:

- Who attended the meeting;
- Action items created during the meeting including who is responsible for the action;
- Any resolution of action items from a previous meeting;
- Any issues or concerns identified during the review of the data with brief rationale for the concern.

5. DATA PROVIDED TO THE COMMITTEE AND PARAMETERS TO BE MONITORED/REVIEWED BY THE COMMITTEE

5.1. C4591001 Study Only

The committee will review all data on a regular basis (see Section 4.1 and below) and during Phase 1 will also review data from the BioNTech German study as it becomes available. Committee reviews will allow early detection of signs of efficacy or disease enhancement

with corresponding early expansion of testing of vaccine candidates, doses, or regimens to larger numbers of subject or, conversely, curtailment of testing for other candidates, doses, or regimens. Immunogenicity data may also be reviewed. The committee chairperson will communicate any required action according to the communication plan (refer to Section 6 *Communication Plan Between Pfizer and the Committee*).

5.1.1. Serious Adverse Events

All SAEs deemed unexpected and related to BNT162 SARS-CoV-2 RNA vaccines, either by the investigator or Pfizer (also known as SUSARs [suspected unexpected serious adverse reactions]), will be forwarded to the committee at the same time as they are reported to the RAs, investigators, and institutional review boards (IRBs)/ethics committees (ECs). The term "unexpected" refers to an event that is either not listed in the Investigator's Brochure (IB) Reference Safety Information section or is of greater severity or specificity than that listed in the IB Reference Safety Information section.

All SAEs collected through 6 months after the vaccination schedule is completed will be reviewed contemporaneously. Additionally, SAE data from the ongoing BioNTech clinical trial (BNT162-01) will be provided to the committee for information during the Phase 1 portion of the C4591001 study as it becomes available to ensure a comprehensive overview of information of the BNT162 vaccines is available.

5.1.2. Other Safety

Cumulative data of reactogenicity events and unsolicited adverse events (including that from the ongoing BioNTech clinical trial as it becomes available in Phase 1) will be reviewed on a regular basis during scheduled committee meetings. Contemporaneous review of related AEs up to 1 month after completion of the vaccination schedule will be performed. In addition, during Phase 2/3 the committee will review all AEs on a weekly basis until safety data through 7 days after dose 2 from the first 360 participants has been submitted to regulatory authorities. The committee will schedule an adhoc meeting if deemed necessary.

The committee will meet as soon as possible to review all available relevant-data when any stopping rule is met. Please refer to sections 8.2.3 and 10.7 of the C4591001 protocol for stopping rules.

5.1.3. Surveillance of Events That Could Represent Enhanced COVID-19 Disease

Because within the course of COVID-19, the illness caused by SARS-CoV-2 infection, the onset of an exaggerated adaptive immune response and containment of viral replication in some instances is associated with a "cytokine storm" that accompanies clinical deterioration,

patient profiles of all nucleic acid amplification test (NAAT)-confirmed cases will be reviewed contemporaneously by the committee during Phase 1 of the study.

In Phase 2/3, there will be planned reviews of the vaccine/placebo split of protocol-defined severe COVID-19 cases at the time of efficacy/futility analyses. The DMC will review this data and make recommendations based on the guidance outlined in Section 10.7 of the protocol: Stopping and alert rules for severe disease defined.

Additionally, in Phase 2/3, the unblinded team supporting the DMC, including an unblinded medical monitor, will review cases of severe COVID-19 as they are received and will review AEs at least weekly for additional potential cases of severe COVID-19. At any point, the unblinded team may discuss with the DMC chair whether the DMC should review cases for an adverse imbalance of cases of COVID-19 and/or severe COVID-19 between the vaccine and placebo groups. If so, the DMC will then meet to review available severe COVID-19 cases to determine whether the observed imbalance should result in modifications to the study. Please refer to section 8.2.4 of the protocol for details.

In addition to the above, data regarding COVID-19 confirmed illnesses reported in the BioNTech study will be reviewed by the committee when information is available.

The purpose of these reviews will be to identify whether any features of each case appear unusual, greater in severity, compared to available information at the time of review. Indicators of severity may include accelerated deterioration, need for hospitalization, need for ventilation, death. Observed rates of these indicators will be compared with what could be expected in a similar population to the study participants based upon available information at the time of review (for Phase 1 and 2/3) and to compare cases in active vaccine and placebo recipients in Phase 2/3 (when Pfizer staff will be blinded).

5.1.4. Immunogenicity

The DMC may review safety and immunogenicity data prior to expansion into Phase 2/3.

5.1.5. Efficacy

The DMC will assess efficacy data for efficacy and/or futility during the Phase 2/3 portion of the C4591001 study as defined in the protocol.

5.2. All Other Studies

Please refer to Appendix 4 for details.

5.2.1. Serious Adverse Events

All SAEs deemed unexpected and related to BNT162 SARS-CoV-2 RNA vaccines, either by the investigator or Pfizer (also known as SUSARs [suspected unexpected serious adverse

reactions]), will be forwarded to the committee at the same time as they are reported to the RAs, investigators, and institutional review boards (IRBs)/ethics committees (ECs). The term "unexpected" refers to an event that is either not listed in the Investigator's Brochure (IB) Reference Safety Information section or is of greater severity or specificity than that listed in the IB Reference Safety Information section.

All SAEs will be reviewed. Studies in which SAEs are followed for longer timepoints may also be reviewed by the committee.

5.2.2. Other Safety

Cumulative data of reactogenicity events, unsolicited adverse events, and clinical laboratory assessments (if applicable) from other studies in the program will be reviewed on a regular basis during scheduled committee meetings, as described in Section 5.1.2. Data may be blinded or unblinded depending on study design.

5.2.3. Immunogenicity

The DMC may review immunogenicity data.

5.2.4. Efficacy

The DMC will assess efficacy and/or futility for all other studies if appropriate.

5.3. Provision of Study Data to the Committee

The reporting statistician is the primary channel for providing output/reports to the committee. Approximately 24 hours to up to 5 calendar days prior to each review meeting the reporting statistician will transmit all appropriate study data (as described in Section 5 *Data Provided to the Committee and Parameters to be Monitored/Reviewed by the Committee*) via secure electronic means to the committee members.

Committee members must handle all study data in accordance with the confidentiality agreement in their contract. Any queries on the data are to be made to reporting statistician and any requests for additional data must be communicated in writing (e.g., meeting minutes) via secure electronic means to the reporting statistician with supporting rationale for such requests. The reporting statistician may consult with the Vaccine Research & Development Clinical and Statistical Heads (or the IRC if applicable) prior to acting upon the request. If the study is blinded, the nature and content of the query requests may not be shared with the study team(s).

5.3.1. Open Session Data

Prior to each review meeting, the committee will receive the following summary data combined across or summarized by the vaccine groups, depending on study phase, regarding the progress of the trials.

- Study conduct issues (e.g., enrollment status, eligibility violations).
- Demographic and other baseline characteristics.
- Dose-escalation decisions made by the IRC as applicable.
- Actions taken by the IRC in response to events that met the stopping rule criteria as applicable.

5.3.2. Closed Session Data

Prior to review meetings, the committee will receive the safety data indicated below summarized/analyzed by vaccine group. Additionally, the committee will receive relevant subject data listings. For blinded studies and or studies with blinded stages/phases, closed sessions will be conducted.

- Study status.
- Demographics.
- Reactogenicity data (up to 7 days post vaccination) when available.
- AEs and SAEs.
- AEs associated with withdrawal.
- Laboratory data when available.
- Significant findings identified by the clinician/clinical lead, who will review blinded safety data as specified in the safety surveillance review plan.
- Significant findings identified by the IRC, who will review unblinded safety data as specified in the IRC charter.
- Data from interim analyses of safety, efficacy, and immunogenicity as defined in the statistical analysis plan.

- The DMC may also review safety signals identified by the JSRT from periodic reviews of the clinical trial data as specified in JSRT charter.

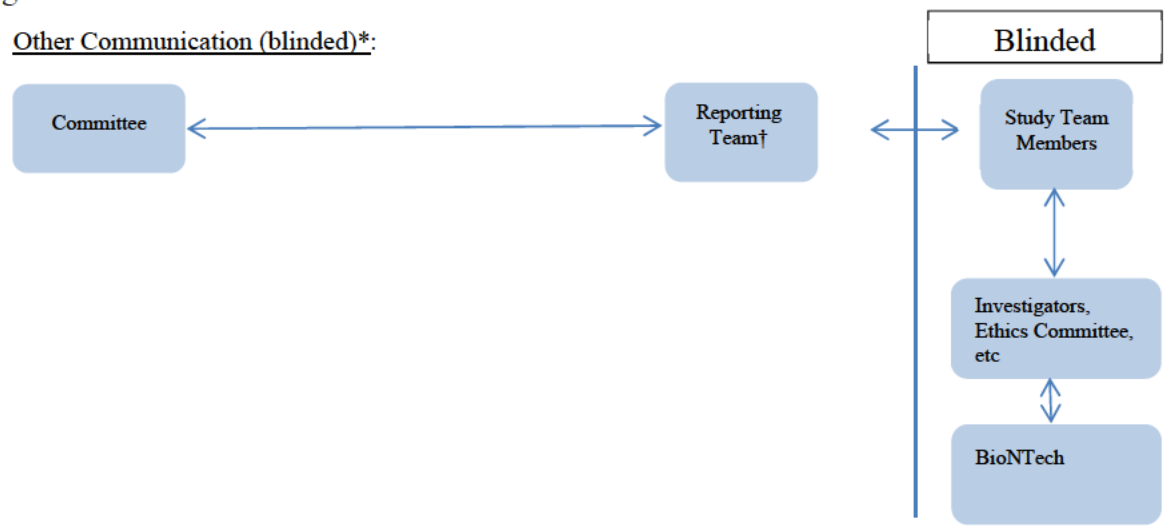
5.4. Database Information

All data provided to the committee will be from a dynamic database that is continually updated or revised as new information becomes available. A copy of the database snapshot used for the reports will be maintained. Tables, listings, and figures will be annotated with the date on which they were generated.

6. COMMUNICATION PLAN BETWEEN PFIZER AND THE COMMITTEE

The expected flow of information and recommendations are depicted in Figure 1.:

Figure 1:



* For example, open session meetings, blinded SAE reports, additional analysis/data requests, committee meeting logistics
† Committee liaison is part of the Reporting Team; During the Phase 2/ 3 portion of the C4591001 study, an unblinded medical monitor and unblinded Clinical Scientist will be included as part of the Reporting Team. Communication between the DMC and study team occurs through the committee liaison during Phase 2/3.
NB. C4591005 is sponsor unblinded throughout

6.1. Recommendations

After each meeting, the committee will provide one of the following recommendations (for each study reviewed) to Pfizer via CT22-GSOP-RF11:

- Withhold final recommendation until further information/data is provided.
- Continue the study or studies as designed.
- Modify the study or studies and continue.
- Stop the study or studies.

Additionally, the committee may be asked to answer study related questions (e.g., concerning operational challenges, impact of findings from Pfizer's safety data review or impact of emerging external information) provided by the study team. The answers to the questions will be provided with the committee recommendation to Pfizer management via the committee liaison.

The recommendations should be in accordance with the guidance provided in this charter, the protocol, or the SAP (or other document, as appropriate, e.g., interim analysis plan).

6.2. Communication of Recommendations

For each review meeting, once a committee recommendation has been finalized the committee chairperson will convey the recommendation in writing within the timelines listed on CT22-GSOP-RF11. The written communication will consist of the CT22-GSOP-RF11 indicating the committee's recommendation and sufficient information to explain the rationale for any recommendation will be transmitted by secure electronic means to the committee liaison.

The final decision to accept or reject the committee's recommendation resides with Pfizer management and will be communicated to the committee chairperson in writing. Review of committee recommendation will be conducted in accordance with CT22-GSOP-RF11.

6.3. External Pfizer Communication

The committee's recommendation, together with Pfizer's response, will be summarized by the study team who will be responsible for communicating to all active investigators participating in the trial and to BioNTech representatives. The investigators and BioNTech will be informed about the decision to continue the trial, to stop the trial, or to implement modifications to trial procedures, on a monthly basis.

6.4. Pfizer Internal Safety Review Committee

Pfizer has established several ad hoc Internal Safety Review Committees (ISRCs), one for each BU/RU. The ISRC for a BU is properly firewalled from all study teams conducting trials sponsored by that unit. The primary objective of an ISRC is to assess specific events that may constitute a safety concern in an unblinded manner. The assessment could result in expedited reports to regulators as required in FDA Final Rule (2010) and EU CT-3 (2011). The assessment may also lead to safety-related protocol changes. When necessary, an ISRC could look at the occurrence of the specific events across multiple studies in a development program.

The activities of an ISRC are intended to be complementary and supplemental to existing Pfizer safety and risk management processes, including this committee. There is a charter for the ISRC describing in detail the purpose, composition, and operations of an ISRC. The charter is available upon request.

There may be several interactions between an ISRC and this committee, including:

- When the ISRC accepts a request from the signal management lead to review specific events, the ISRC chair will notify the committee chairperson that a request has been made and that a review is to be conducted with a target date (typically within 30 calendar days of the request).
- The committee liaison will supply the ISRC chair a copy of the current committee charter, open meeting minutes and correspondences from the committee regarding issues for which the ISRC is currently being consulted.
- ISRC chair will communicate review findings with the committee chairperson.
- If no safety concern is identified, the ISRC will communicate this conclusion to the signal management lead with a copy to the committee.
- If a safety concern is identified, the ISRC chair will communicate its findings to the committee chairperson by an appropriately secure means. The written communication contains the ISRC's rationale and final assessment. (As the findings are typically based on unblinded data, they must not be shared with the study team at this stage.)
- The committee chairperson is requested to acknowledge receipt of the ISRC communication as soon as possible. The committee considers the findings identified by the ISRC but is not obligated to act on them.

- Where disagreement exists between the recommendations of the ISRC and the committee, the two committees attempt to reach consensus through additional communication.

- The final decision to accept or reject the committee's and/or ISRC's recommendation resides with Pfizer management.

- The safety data (tables, listings, and reports, etc.) received by the ISRC for review are kept confidential and will be disclosed to the committee upon request from the committee chairperson.

7. WRITTEN RECORDS

The committee liaison will maintain written records of all closed session meeting minutes, CT22-GSOP-RF11, and materials reviewed by the committee, and communications between the committee and Pfizer. These documents are considered proprietary and confidential and must be available for inspection upon request from RAs. Upon completion of the committee's responsibilities, the study team will obtain all written records for archiving.

7.1. Deliverables to Pfizer

The following are the deliverables from the committee chairperson to the committee liaison.

After each committee review meeting:

- CT22-GSOP-RF11.

- Closed session meeting minutes.

7.2. General Project File

The study team will compile and maintain the following documents and correspondence throughout study conduct.

- Any relevant correspondence between the committee and Pfizer.

- Committee charter and any amendments.

- Current IB.

- Protocol and protocol amendments.

- Curriculum vitae for each committee member.

- CT22-GSOP-RF01 for each committee member.
- Minutes from each open session meeting.

7.3. Unblinded data in SAS® Datasets

The treatment assignment blind will not be broken in the project database **for Phase 2/3 of the study**. The unblinded treatment assignment information will be merged programmatically with the study datasets using SAS®. Unblinded SAS® datasets and program files will be stored and managed in an area that is separate from the general project area and inaccessible except to members of the reporting team.

8. CHARTER HISTORY

Version	Date (dd-Mmm-yyyy)	Summary of Changes
1	29-Apr-2020	N/A
2	10-Jul-2020	Updated to reflect Protocol Amendment 4 (C4591001*)
3	17-Aug-2020	Updated to reflect Protocol Amendment 5 (C4591001*)
4	22-Oct-2020	Updated to include C4591005 Japan Study
5	04-Nov-2020	Updated to include 3 additional Programmers and an unblinded Clinical Scientist to the Reporting Team
6	25-Jan-2021	Updated to include C4591007, C4591015, C4591017 and C4591020
7	05-Feb-2021	Updated to reflect change in Reporting Team personnel
8	17-Mar-2021	Updated to include OBGYN DMC Consultants, Dr Robert Heine and Dr Heather Lipkind. Added C4591018 and C4591024
9	31-Mar-2021	Updated to remove C4591018, amend the study title for C4591024, and add study C4591028
10	05-May-2021	Updated to reflect changes in Reporting Team and Study Team personnel
11	17-May-2021	Updated to include B7471026, moved study details from Section 5.2 to Appendix 4 and updated study team personnel details. Removed C4591028 due to study halt.

12	11-Jun-2021	Added study C4591031
13	16-Jul-2021	Updated study team personnel changes

* Protocol Amendments 1, 2, 3, 6-11 did not result in changes to the Charter, however were shared with the DMC for information.

Appendix 1. Committee Membership Log

The following outlines the key selection criteria for membership into the E-DMC:

- Relevant clinical, region and/or drug development expertise
- Expert in the field of Infectious Diseases and/or Statistics
- Experience serving on a DMC
- Required time commitment based on the scope of responsibilities

The committee consists of the following members (past and present).

Member	Affiliation/Address	Role	*Dates of Membership	Biography
Jonathan Zenilman, MD	Infectious Diseases Division Johns Hopkins Bayview Medical Center Baltimore, MD, US Tel: +1 410 440 9729	Chair	03-April-2020	Infectious Diseases
Kathryn Edwards, MD	Vanderbilt University School of Medicine 1300 Falkirk Court, Nashville, TN 37221 Tel: +1 615-429-3226	E-DMC member	07-April-2020	Pediatric infectious Diseases
Robert Belshe, MD	Division of Infectious Diseases & Immunology Saint Louis University Medical Center 714 Schiele Ave, San Jose, CA 95126 Tel: +1 314 496 1033	E-DMC member	03-April-2020	Infectious Diseases and Immunology
Lawrence Stanberry, MD	Columbia University 456 Riverside Drive, Apt 8A, New York, NY, 10027 Tel: +1 646-330-8329	E-DMC member	07-April-2020	Pediatric Infectious Diseases
Steve Self, PhD	Fred Hutchinson Cancer Research Center Vaccine and Infectious Disease Division 1100 Fairview Avenue North, M2- C200, Seattle, WA 98109, USA Tel: +1 206-915-9617	E-DMC Biostatistician	02-April-2020	Professor Emeritus, Biostatistics

Robert Philips Heine, MD	Wake Forest Baptist Health 2555 Bitting Road Winston-Salem, NC 27104 Tel: +1 919-602-3066	E-DMC member	18-February 2021	Obstetrics, Maternal Fetal Medicine
Heather S Lipkind, MD, MS	Department of Obstetrics, Gynecology, and Reproductive Sciences Yale University, New Haven, CT Tel: +1 203-643-6992	E-DMC member	18-February-2021	Associate Professor: Maternal Fetal Medicine, Department of Obstetrics, Gynecology, & Reproductive Sciences

* Initial date of membership is the date the effective date of the contract signed by the committee member.

Note: Curriculum vitae are on-file at Pfizer and may be accessed by contacting the Study Team.

Appendix 2. Plan to Control Dissemination of Results

For studies that require such a plan, this will be documented in a study-level document that will be filed in the TMF.

Appendix 3. Key Contacts

Vaccine Research & Development Clinical and Statistical Heads	
Name*	***Contact Information***
William Gruber, MD	Senior Vice President, Vaccine Clinical Research & Development 401 N Middletown Road Pearl River, NY 10965 USA Tel: +1 845-602-3484 Bill.Gruber@Pfizer.com
Stephen Lockhart MD	Vice President Head of Europe and Asia-Pacific, Vaccine Clinical Research and Development Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Tel: +44 1628 515538 Stephen.P.Lockhart@pfizer.com
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Committee Liaison	
Name*	***Contact Information***
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Loredana Popia	1030 Sync Street Morrisville, NC 27560 United States loredana.popia@syneoshealth.com

Reporting Team Members (Unblinded)*		
Name*	***Contact Information***	***Role***
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WeiWei Xiong	Senior Associate Pfizer, Inc 500 Arcola Road Collegeville PA 19426 USA	Statistical Programming

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Sridhar Guduru	Senior Statistical Programming Lead Manager Pfizer, Inc 500 Arcola Road Collegeville PA 19426 USA Sridhar.Guduru@pfizer.com	Statistical Programming
Chris Webber MD	Senior Director Vaccine Clinical Research and Development Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Tel: +44 7879 800869 chris.webber@pfizer.com	Unblinded Medical Monitor
Lisa Moyer**	Senior Manager Pfizer, Inc 500 Arcola Road Collegeville PA 19426 USA Tel: +1 (484) 8658348 Lisa.L.Moyer@pfizer.com	Unblinded Clinical Scientist

* The Reporting Team comprises of a number of supporting/back-up Statistical Programmers across the C459 program. Full details of supporting staff can be located in a separate staffing document.

** The unblinded Clinical Scientist (CS) will assist with responding to subject level queries using relevant data systems during DMC closed sessions, whilst the unblinded medical

monitor (MM) is required to address medical questions and interpretation. The MM and CS are complimentary and the pairing mimics how Pfizer typically conduct safety reviews for clinical trials for all studies.

Study Team Members		
Name*	***Contact Information***	***Role***
Nicholas Kitchin, MD	Senior Director, Vaccine Clinical Research and Development Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Tel : +44 7557 202435 nicholas.kitchin@pfizer.com	Clinical Study Lead
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Alejandra Gurtman, MD	Vice President Pfizer Vaccine Clinical Research and Development	Study Clinician

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Harpreet Seehra	Senior Manager, Clinical Scientist Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Tel: +44 7901788821 harpreet.seehra@pfizer.com	DMC Responsible Clinical Scientist
Xia Xu	Senior Director Pfizer, Inc 500 Arcola Road Collegeville PA 19426	Xia Xu (Program Biostatistician

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Juleen Gayed, MD	Director, Clinician Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom	Study Clinician C4591017

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Sohil Patel, MD	Associate Director, Clinician Horizon Building Honey Lane Hurley SL6 6RJ United Kingdom Sohil.Patel@pfizer.com	Study Clinician C4591020
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Mariano Young, MD	Senior Director Pfizer, Inc 500 Arcola Road	Study Clinician B7471026

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Appendix 4. List of Studies (if committee is to oversee multiple studies)

Study	Date Added (dd-Mmm-yyyy)
C4591001: A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study To Evaluate The Safety, Tolerability, Immunogenicity, And Efficacy Of SARS-COV-2 RNA Vaccine Candidates Against COVID-19 In Healthy Individuals	29-Apr-2020
C4591005: A Phase 1/2, Placebo-controlled, Randomized, and Observer-blind Study to Evaluate the Safety, Tolerability, and Immunogenicity of a SARS-COV-2 RNA Vaccine Candidate Against COVID-19 in Healthy Japanese Adults	22-Oct-2020
C4591007: A Phase 1 Open Label Dose-Finding Study To Evaluate Safety, Tolerability And Immunogenicity And Phase 2/3 Placebo-Controlled, Observer Blinded Safety, Tolerability, And Immunogenicity Study of a SARS-COV-2 RNA Vaccine Candidate Against COVID-19 In Healthy Children <12 Years of Age	18-Jan 2021
C4591015: A Phase 2/3, Placebo-Controlled, Randomized, Observer-Blind Study To Evaluate The Safety, Tolerability, And Immunogenicity Of a SARS-COV-2 RNA Vaccine Candidate (BNT162b2) Against COVID-19 In Healthy Pregnant Women 18 Years Of Age And Older	18-Jan 2021
C4591017: A Phase 3, Randomized, Observer-Blind Study To Evaluate The Safety, Tolerability, And Immunogenicity Of Multiple Production Lots And Dose Levels Of The Vaccine Candidate BNT162b2 Against COVID-19 In Healthy Participants 12 Through 50 Years Of Age	18-Jan-2021
C4591020: A Phase 3, Randomized, Observer-Blind Study To Evaluate The Safety, Tolerability, And Immunogenicity Of a Lyophilized Formulation Of The Vaccine Candidate BNT162b2 Against COVID 19 In Healthy Adults 18 Through 55 Years Of Age	18-Jan 2021
C4591024: A Phase 2B, Open Label Study To Evaluate Safety, Tolerability And Immunogenicity Of Vaccine Candidate	17-Mar-2021

BNT162B2 In Immunocompromised Participants ≥ 2 Years Of Age	
B7471026: A Phase 3, Randomized, Double Blind Trial To Describe The Safety And Immunogenicity Of 20 Valent Pneumococcal Conjugate Vaccine When Coadministered With A Booster Dose Of BNT162b2 In Adults 65 Years Of Age And Older	17-May-2021
C4591031: A Phase 3 Master protocol to Evaluate Additional Dose(s) Of BNT162b2 in Healthy Individuals Previously Vaccinated with BNT162b2	11-June-2021

Please refer to the current C4591001, C4591005, C4591007, C4591015, C4591017, C4591020, C4591024, B7471026 and C4591031 protocols for details of the study designs.